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CLAIMS

We claim:

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1. A compound of the general formula:

$$R_a$$
 R_b
 R_{h1}
 R_{h2}
 R_{h2}

wherein:

- a) R_b and R_0 are independently -H, unless otherwise noted to be -Cl, -Br, -I, -F, -CN, lower alkyl, -OH, -OR₆,-CH₂-OH, -NH₂, or N(R₆)(R₇), wherein R₆ and R₇ are independently hydrogen or an alkyl or branched alkyl with up to 10 carbons;
- b) R_a is -N₃, -C=N, -CH₂-C=R, -C=C-R, -C=CH-R, -R-C=CH₂, -C=CH, -CH₂-C=N, -C(H)-C(O)-OR₃, -O-R, -R-R₁, -O-R-R₁, OR(O)R, OR(O)R₁, ROR, ROR₁, -NHC(O)R₆, -NRC(O)R₆, -NH₂, or N(R₆)(R₇), wherein R₆ and R₇ are independently hydrogen or an alkyl or branched alkyl with up to 10 carbons; or a hetero group wherein the hetero group may have more than one hetero atom and may be substituted, where R is H or a straight or branched alkyl with up to 10 carbons or aralkyl, and in any position F may be substituted in or on the carbon chain, and R₁ is -OH, -NH₂, -Cl, -Br, -I, -F or CF₃ when R₁ is terminal;
 - c) Z' is >COH, unless otherwise noted to be >C-OAc;
- d) >C-Rg is >CH₂, >C(H)-OH, >C=O, >C=N-OH, >C(R₃)OH, >C=N-OR₃, >C(H)-NH₂, >C(H)-NHR₃, >C(H)-NR₃R₄, or >C(H)-C(O)-R₃, where each R₃ and R₄ is independently an alkyl or branched alkyl with up to 10 carbons or aralkyl; or
- Rg is i) an alkyl of 1-10 carbon atoms that is straight chain or branched, ii) an alkenyl of 1-10 carbon atoms that is straight chain or branched having one or more double bonds at

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any position from C to Zo, iii) an alkenyl group of 1-10 carbon atoms that is straight chain or branched having one or more triple bonds at any position where chemically possible, iv) a mono or dialkyl amino group wherein each alkyl chain has from 1-10 carbon atoms and is straight chain or branched, v) (CH₂)_n-CF₂-, (CH₂)_n-CR₁ or (CH₂)_n-CF₃ wherein n=0-10 carbons, or vi) H, and wherein any of i-iv are optionally substituted with an aromatic or heteroaromatic group or optionally substituted with a heterogroup and wherein Rg is either in the α or β position and; or

 R_g is Rg_1 and Rg_2 , and wherein Rg_1 may be present or absent and when present is -H, an alkyl, alkenyl, or alkynyl of 1-10 carbon atoms that is straight chain or branched and is optionally substituted, and Rg_2 is a hetero group, wherein when Rg_1 is absent the heterogroup is bonded to the 17-position with a double bond, and wherein either Rg_1 or Rg_2 can be in the β position with the other group in the α position, and R_1 is -OH, $-NH_2$, -Cl, -Br, -I, -F or CF_3 when R_1 is terminal;

e) R_{h1} and R_{h2} are independently H, unless otherwise noted to be a straight or branched chain alkyl, alkenyl or alkynyl with up to 10 carbons that is unsubstituted, or substituted with one or more groups selected from a hetero functionality that is either not substituted, monosubstituted or multiply substituted with an alkyl, alkenyl or alkynyl chain up to 10 carbons; a halo functionality (F, Cl, Br or I); an aromatic group optionally substituted with at least one hetero, halo or alkyl; of R_{h1} and R_{h2} are independently a group containing at least one alphatic or aromatic group optionally substituted with at least one hetero, halo or alkyl;

f) Z" is >CH2;

and wherein saturated bonds in any ring may be dehydrogenated;

and wherein all monosubstituted substituents have either an α or β configuration;

and wherein lower alkyl is defined as a carbon chain having 1-10 carbon atoms which may be branched or unbranched.

2. The compound of Claim 1, wherein:

Ra is -OCH3; and

 R_{g1} and R_{g2} are each H.

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3. The compound of Claim 1, wherein:

Ra is -OCH3; and

 R_g is = CH_2 .

4. The compound of Claim 1, wherein:

Ra is -OCH3;

Rg₁ is absent; and

5 R_{g2} is =NOH.

5. The compound of Claim 1, wherein:

Ra is -OCH3;

Rg₁ is β -H₁; and

10 R_{g2} is α -OH.

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6. The compound of Claim 1, wherein:

Ra is -OCH3;

Rg₁ is -H; and

Rg2 is -NH2.

7. The compound of Claim 1, wherein:

Ra is -OCH3;

Z' is >C-OAc;

Rg₁ is -H; and

R_{g2} is -OAc.

8. The compound of Claim 1, wherein:

Ra is -OCH3;

25 Rg₁ is –H; and

Rg2 is -CH2CH2CH3.

9. The compound of Claim 1, wherein:

Ra is -OCH3;

 Rg_1 is -H; and

Rg2 is -CH3.

10. The compound of Claim 1, wherein:

Ra is -OCH3; and

 R_g is =CHCH2CH3.

5 11. The compound of Claim 1, wherein:

Ra is -OCH3;

 Rg_1 is -H; and

 R_{g2} is -NHCH₂CH₂CH₃.

10 12. The compound of Claim 1, wherein:

Ra is -OCH3; and

 R_g is =CHCH3.

13. The compound of Claim 1, wherein:

Ra is -OCH3;

 Rg_1 is -H; and

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Rg2 is -CH2CH3.

14. The compound of Claim 1, wherein:

Ra is -OCH3; and

 R_g is =N-NH-(SO₂)-C₆H₄-*p*-CH₃.

15. The compound of Claim 1, wherein:

R_a is -OCH₃;

Rg1 is H; and

R_g2 is -COOH.

- 16. A method of modifying estradiol analogs for preventing or hindering demethylation, oxidation and conjugation with another molecule during metabolism.
- 17. The method claim 16 wherein the method comprises adding steric bulk or modification of chemical or electrostatic characteristics or a combination thereof to estradiol analogs for retarding or preventing metabolic deactivation.

$$>$$
C-R_{g1} is $>$ CH;

$$>$$
C-R_{g2} is $>$ COH; and

 R_{h1} and R_{h2} are independently -H and Et.

19. The compound of Claim 1, wherein:

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R_{h1} and R_{h2} are independently H and n-Pr.

20. The compound of Claim 1, wherein:

$$>$$
C-R_{g1} is $>$ CH;

 R_{h1} and R_{h2} are independently H and i-Bu.

21. The compound of Claim 1, wherein:

$$>$$
C-R_{g1} is $>$ CH;

R_{h1} and R_{h2} are independently H and CH₂OH.

22. The compound of Claim 1, wherein:

$$>$$
C-R_{g1} is $>$ CH;

 R_{h1} and R_{h2} are independently H and n-Bu.

Ra is -OCH3;

>C-R_{g1} is >CH;

>C-R_{g2} is >COH; and

5 Z" is >CH2, and

 $R_{h1} \ \text{and} \ R_{h2}$ are independently H and Me.

24. The compound of Claim 1, wherein:

Ra is -OCH3;

10 >C-R_{g1} is >CH;

>C-R_{g2} is >COH; and

 R_{h1} and R_{h2} are independently H and -CH₂N(CH₃)₂.

25. The compound of Claim 1, wherein:

 R_a is $-C(O)CH_3$;

>C-Rg1 is >CH; and

>C-R_{g2} is >COH.

26. The compound of Claim 1, wherein:

 R_a is -C(O)H;

>C-Rg1 is >CH; and

>C-R_{g2} is >COH.

27. The compound of Claim 1, wherein:

25 R_a is -CH₂OH;

>C-Rg1 is >CH; and

>C-R_{g2} is >COH.

28. The compound of Claim 1, wherein:

 R_a is $-NO_2$;

>C-Rg1 is >CH; and

>C-R_{g2} is >COH.

29. The compound of Claim 1, wherein:

 R_a is $-N(CH_3)_2$;

>C-Rg1 is >CH; and

5 >C-R_{g2} is >COH.

30. The compound of Claim 1, wherein:

Ra is -NH2;

>C-R_{g1} is >CH; and

10 >C-R_{g2} is >COH.

31. The compound of Claim 1, wherein:

 R_a is $-C \equiv C - CH_3$;

>C-Rg1 is >CH; and

>C-R_{g2} is >COH.

32. The compound of Claim 1, wherein:

Ra is -CH2CH3;

>C-Rg1 is >CH; and

>C-R_{g2} is >COH.

33. The compound of Claim 1, wherein:

Ra is -CH3;

>C-Rg1 is >CH; and

25 >C-R_{g2} is >COH.

34. The compound of Claim 1, wherein:

Ra is -NH2; and

 R_{g1} and R_{g2} are each H.

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- 5 36. The compound of Claim 1, wherein : $R_a \text{ is -NH2}^+\text{CH3}; \text{ and}$ $R_{g1} \text{ and } R_{g2} \text{ are each H}.$
- 37. The compound of Claim 1, wherein:

 Ra is -N(CH3)2; and

 Rg1 and Rg2 are each H.
 - 38. The compound of Claim 1, wherein:

 Ra is -NH⁺(CH3)2 (or N(CH3)2[•]HCl); and

 Rg1 and Rg2 are each H.
 - 39. The compound of Claim 1, wherein:

 R_a is -NH⁺(CH₃)₂ or N(CH₃)₂-HCl; and

 >C-R_{g1} is >CH; and

 >C-R_{g2} is >COH.
- 41. The compound of Claim 1, wherein: $R_a \text{ is -OCH}_2\text{CH}_3;$ $R_g 1 \text{ is absent; and}$ $R_g 2 \text{ is =CHCH}_3.$

The compound of Claim 1, wherein: 42. R_a is $-C \equiv C - CH_3$; Rg1 is absent; and $R_g 2 = CHCH_3$. 5 The compound of Claim 1, wherein: 43. R_a is -C(O)H; R_g1 is absent; and $R_g 2 = CHCH_3$. 10 The compound of Claim 1, wherein: 44. R_a is -NHC(O)H or -NNC(O)N; Rg1 is absent; and $R_g2 = CHCH_3$. The compound of Claim 1, wherein: 45. Ra is -CH2OH; Rg1 is absent; and $R_g 2 = CHCH_3$. The compound of Claim 1, wherein: 46. R_a is -CH₂CH₃; Rg1 is absent; and $R_g 2 = CHCH_3$. 25 The compound of Claim 1, wherein: 47. R_a is $-CH_3$;

Rg1 is absent; and

 $R_g 2 = CHCH_3$.

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The compound of Claim 1, wherein:
       48.
               R<sub>a</sub> is -CH=CHCH<sub>3</sub>;
               R<sub>g</sub>1 is absent; and
               R_g 2 = CHCH_3.
 5
               The compound of Claim 1, wherein:
       49.
               R<sub>a</sub> is -OCH<sub>2</sub>CH<sub>3</sub>;
               R<sub>g</sub>1 is absent; and
               R_g 2 = CH_2.
10
               The compound of Claim 1, wherein:
       50.
                R_a is -C \equiv CCH_3;
Rg1 is absent; and
                R_g2 = CH_2.
                The compound of Claim 1, wherein:
        51.
                R_a is -C(O)H;
                Rg1 is absent; and
                R_g 2 = CH_2.
                The compound of Claim 1, wherein:
        52.
                R_a is -NHC(O)H;
                Rg1 is absent; and
                R_g 2 = CH_2.
 25
                The compound of Claim 1, wherein:
        53.
                 Ra is -CH2OH;
                Rg1 is absent; and
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 $R_g 2 = CH_2$

	54.	The compound of Claim 1, wherein:
		R_a is $-CH_2CH_3$;
		R _g 1 is absent; and
		$R_g 2 = CH_2$
5		
	55.	The compound of Claim 1, wherein:
		R_a is $-CH_3$;
		R _g 1 is absent; and
		$R_g 2 = CH_2$
10		
	56.	The compound of Claim 1, wherein:
		R _a is –CH=CHCH ₃ ;
		R _g 1 is absent; and
		$R_g 2 = CH_2.$
15		
	57.	The compound of Claim 1, wherein:
		R_a is $-OCH_2CH_3$; and
		R _g 1 and R _g 2 are each H.
11 20 1		
20	58.	The compound of Claim 1, wherein:
		R _a is -C≡CCH ₃ ; and
		$R_g 1$ and $R_g 2$ are each H.
	50	m
2.5	59.	The compound of Claim 1, wherein:
25		R _a is -C(O)H; and
		$R_g 1$ and $R_g 2$ are each H.

The compound of Claim 1, wherein:

 R_a is -NHC(O)H; and

 $R_{\rm g}1$ and $R_{\rm g}2$ are each H.

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The compound of Claim 1, wherein: 61. R_a is -CH₂OH; and $R_{\rm g}1$ and $R_{\rm g}2$ are each H.

- The compound of Claim 1, wherein: 5 62. Ra is -CH2CH3; and Rg1 and Rg2 are each H.
- The compound of Claim 1, wherein: 63. R_a is -CH₃; and 10 Rg1 and Rg2 are each H.
- The compound of Claim 1, wherein: 64. Ra is -CH=CHCH3; and Rg1 and Rg2 are each H.
 - The compound of Claim 1, wherein: 65. R_a is -OCH₂CH₃; Rg1 is H; and R_g2 is CH_3 .
 - The compound of Claim 1, wherein: 66. R_a is $-C \equiv CCH_3$; Rg1 is H; and R_g2 is CH_3 .
- The compound of Claim 1, wherein: 67. R_a is -C(O)H; Rg1 is H; and 30 R_g2 is CH₃.

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The compound of Claim 1, wherein:
        68.
                 R_a is -NHC(O);
                 Rg1 is H; and
                 R<sub>g</sub>2 is CH<sub>3</sub>.
 5
                 The compound of Claim 1, wherein:
        69.
                 R_a is -CH_2OH;
                 Rg1 is H; and
                 R<sub>g</sub>2 is CH<sub>3</sub>.
10
        70.
                  The compound of Claim 1, wherein:
                  Ra is -CH2CH3;
Rg1 is H; and
                 R_g2 is CH_3.
                  The compound of Claim 1, wherein:
        71.
                  R_a is -CH_3;
                  Rg1 is H; and
                  R<sub>g</sub>2 is CH<sub>3.</sub>
                  The compound of Claim 1, wherein:
        72.
                  R<sub>a</sub> is -CH=CHCH<sub>3</sub>;
                  Rg1 is H; and
                  R<sub>g</sub>2 is CH<sub>3.</sub>
 25
         73.
                  The compound of Claim 1, wherein:
                  R<sub>a</sub> is -OCH<sub>2</sub>CH<sub>3</sub>;
                  Rg1 is H; and
                  R<sub>g</sub>2 is CH<sub>2</sub>CH<sub>3.</sub>
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The compound of Claim 1, wherein:
         74.
                    R_a is -C \equiv CCH_3;
                    R<sub>g</sub>1 is H; and
                    R<sub>g</sub>2 is CH<sub>2</sub>CH<sub>3.</sub>
  5
                    The compound of Claim 1, wherein:
         75.
                    R_a is -C(O)H;
                     R<sub>g</sub>1 is H; and
                     R<sub>g</sub>2 is CH<sub>2</sub>CH<sub>3.</sub>
10
                     The compound of Claim 1, wherein:
          76.
                     R<sub>a</sub> is -NHC(O)H;
R<sub>g</sub>1 is H; and
                     R<sub>g</sub>2 is CH<sub>2</sub>CH<sub>3.</sub>
                     The compound of Claim 1, wherein:
          77.
                     R<sub>a</sub> is -CH<sub>2</sub>OH;
                     R<sub>g</sub>1 is H; and
                     R<sub>g</sub>2 is CH<sub>2</sub>CH<sub>3.</sub>
                     The compound of Claim 1, wherein:
           78.
                      R<sub>a</sub> is -CH<sub>2</sub>CH<sub>3</sub>;
                      R<sub>g</sub>1 is H; and
                      R<sub>g</sub>2 is CH<sub>2</sub>CH<sub>3.</sub>
 25
                      The compound of Claim 1, wherein:
           79.
                      Ra is -CH3;
                      Rg1 is H; and
                      R<sub>g</sub>2 is CH<sub>2</sub>CH<sub>3.</sub>
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80. The compound of Claim 1, wherein: R_a is -CH=CHCH₃; R_g1 is H; and R_g2 is CH₂CH_{3.} 5 81. The compound of Claim 1, wherein: R_a is $-OCH_2CH_3$; Rg1 is absent; and R_g2 is =CHCH₂CH₃. 10 The compound of Claim 1, wherein: 82. R_a is $-C \equiv CCH_3$; Rg1 is absent; and R_g2 is =CHCH₂CH₃. The compound of Claim 1, wherein: 83. R_a is -C(O)H; Rg1 is absent; and R_g2 is =CHCH₂CH₃. The compound of Claim 1, wherein: 84. R_a is -NHC(O)H; Rg1 is absent; and R_g2 is =CHCH₂CH₃. 25 The compound of Claim 1, wherein: 85. R_a is -CH₂OH; Rg1 is absent; and

 R_g2 is =CHCH₂CH₃.

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86. The compound of Claim 1, wherein: R_a is $-CH_2CH_3$; Rg1 is absent; and R_g2 is =CHCH₂CH₃. 5

87. The compound of Claim 1, wherein:

R_a is -CH₃;

Rg1 is absent; and

 R_g2 is =CHCH₂CH₃.

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The compound of Claim 1, wherein: 88.

R_a is -CH=CHCH₃;

Rg1 is absent; and

 R_g2 is =CHCH₂CH₃.

The compound of Claim 1, wherein: 89.

R_a is -OCH₃;

R_g1 is H; and

R_g2 is -CH₂OH.

The compound of Claim 1, wherein: 90.

Ra is -OCH3;

>C-R_{g1} is >CH;

>C- R_{g2} is >COH; and

an olefin at C6-C7. 25

> The compound of Claim 1, wherein: 91.

> > Ra is -N3; and

>C-Rg is >CH.

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The compound of Claim 1, wherein: 90.

Ra is -H; and

>C-R_g is >CH.